UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

IN RE BRISTOL-MYERS SQUIBB SECURITIES LITIGATION	:	Civil Action No. 00-1990 (SRC)
	:	Return Date: June 6, 2005

LEAD PLAINTIFF'S MEMORANDUM OF LAW IN SUPPORT OF ITS MOTION *IN LIMINE* TO EXCLUDE TESTIMONY OF DEFENDNATS' FDA REGULATORY PROCESS EXPERTS, DRS. HEIDI M. JOLSON, STEPHEN FREDD AND JEFFREY ANDERSON, ON DAUBERT GROUNDS AND TO STRIKE THIS TESTIMONY FROM DEFENDANTS' SUMMARY JUDGMENT RECORD

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PRELIMINARY STATEMENT

Lead Plaintiff, the LongView Collective Investment Fund ("Lead Plaintiff"), respectfully submits this memorandum of law in support of its motion *in limine*, pursuant to Fed. R. Evid. 104 and 702 through 704, to exclude certain testimony of defendants' three "FDA Regulatory Process" experts, Drs. Heidi M. Jolson, Stephen Fredd and Jeffrey Anderson, and to strike that inadmissible testimony from defendants' summary judgment record. Defendant Bristol-Myers Squibb ("BMS" or the "Company"), along with individual defendants Charles A. Heimbold ("Heimbold"), Peter R. Dolan ("Dolan") and Peter S. Ringrose ("Ringrose") (collectively, "Defendants"), have proffered expert reports from 18 witnesses in support of their joint motion for summary judgment and defenses in this action.[1]

In light of the recent submission of papers in support of and opposition to Defendants' motion for summary judgment and the Court's August 30, 2004 opinion, familiarity with the facts underlying the claims is presumed. Dr. Jolson has submitted a report to

> opine on the regulatory process for the review of an Investigational New Drug Application ("IND"), and a New Drug Application ("NDA") by the United States Food and Drug Administration ("FDA" or the "Agency"), BMS's compliance with the FDA regulations in the development of Vanlev (a drug compound with the generic name of "omapatrilat") and in its submission of the NDAs for omapatrilat and the FDA's review of omapatrilat.

(DX 17 ¶ 1.)

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[1]Defendants' expert reports were submitted as exhibits 11-28 to the Declaration of Samira Shah, Esq. in Support of Defendants' Motion for Summary Judgment, dated December 17, 2004. To the extent any exhibits cited herein were submitted in support or opposition to Defendants' summary judgment motion, they will be referred to as either "PX" or "DX" and will bear their original summary judgment reference number. Any new exhibits, which were not submitted either in support or opposition to Defendants' summary judgment motion, are being submitted herewith as exhibits to the Declaration of James W. Johnson, Esq. In Support of Lead Plaintiff's Motions *In Limine* to Exclude Testimony of Defendants' Expert Witnesses on Daubert Grounds and to Strike Such Testimony From Defendants' Summary Judgment Motion, dated May 13, 2005 ("Johnson Decl."), and are referred to as "Pl. Ex. ___."

Lead Plaintiff seeks to exclude two portions of Dr. Jolson's expert : (1) her opinion that it was reasonable for BMS to conclude, following the unblinding of OCTAVE, that Vanlev would be approved; and (2) her opinion that Vanlev was approvable, based on the October 11, 2002 "action" letter from the FDA. Both of these opinions do not meet Daubert standards since they are unreliable. These opinions are based on nothing more than impressions formed by Dr. Jolson following a review of limited documents; that review, as acknowledged by Dr. Jolson in her deposition, did not include crucial, material documents that undermined or contradicted her "impressions."

Dr. Anderson submitted a report generally addressing Vanlev's "promise," with particular emphasis on the OCTAVE and OVERTURE trials, and addressing the nature of BMS's communications with FDA. Lead Plaintiff seeks to exclude five portions of Dr. Anderson's report. First, Dr. Anderson does not have the experience or qualifications to comment on what inferences, if any, can be drawn from the fact that the FDA did not rescind the priority review status of the initial Vanlev NDA. Second, Dr. Anderson does not have the education or training to opine on the role that genetics may or may not play with respect to the development of angioedema in patients exposed to Vanlev. Third, Dr. Anderson's opinions as to the FDA's interpretation of the Vanlev risk-benefit ratio, and the FDA's state of mind with respect to the development of the ACE-inhibitor Captopril, must be stricken as they are unreliable and not based on sufficient facts. Finally, two of Dr. Anderson's opinions are unreliable because they are based on one-sided data pre-selected by Defendants.

Dr. Fredd submitted a report to, inter alia:

> address the regulatory process for the review of a New Drug Application ("NDA") by FDA, and on [the FDA Division of Cardio-Renal Drug Products'] review of the NDA for Vanlev.

(DX 13 ¶ 11.) Dr. Fredd further asserts that one small snippet of testimony from the July 2002 advisory committee meeting on Vanlev "would carry great weight" with the FDA's Dr. Robert Temple. (DX13 ¶ 34.) Dr. Fredd also claims that the FDA's Division of Cardio-Renal Drug Products "was more risk averse during their review of the Vanlev NDA than previously in the wake of the withdrawal of Posicor shortly after being approved." (DX13 ¶ 15.) With respect to the clinical trial design discussed in the FDA's October 11, 2002 "action" letter, Dr. Fredd further opined that "a study in resistant hypertension is a feasible study, and the approvable letter included an offer by FDA to assist the company in designing the study." (DX 13 ¶ 97.)

Lead Plaintiff seeks to exclude five areas of Dr. Fredd's report. First, because Dr. Fredd had no involvement with the Vanlev NDA, he cannot opine on the issue of what the FDA knew or believed with respect to the Vanlev NDA. Second, Dr. Fredd has no basis for offering an expert opinion with respect to what Dr. Temple personally thought or believed. Third, Dr. Fredd's opinions with respect to how the "FDA's emphasis on risks and benefits have changed over time," and more specifically with respect to the Division of Cardio-Renal Drug Products becoming "more risk averse during their review of the Vanlev NDA than previously in the wake of the withdrawal of Posicor" (DX13 ¶¶ 14,15) have no basis in fact. Indeed, a key fact Dr. Fredd relies upon in support of his opinions is simply wrong. Fourth, Dr. Fredd does not have the expertise necessary to opine on the feasibility of the clinical trial discussed in the FDA's October 11, 2002 "action" letter.

ARGUMENT

I. Legal Standards Governing Admission of Expert Testimony

Rules 702 through 704 of the Federal Rules of Evidence govern the admissibility of expert testimony, subject to the relevancy provisions of Rules 401 through 403. Rule 702 provides:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

Fed. R. Evid. 702. The rule was amended in 2000 in response to Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579 (1993), and to the many cases applying Daubert, including Kumho Tire Co. v. Carmichael, 526 U.S. 137 (1999) and General Elec. Co. v. Joiner, 522 U.S. 136, 140 (1997). More recently, in Schneider v. Fried, 320 F.3d 396, 405 (3d Cir. 2003), the Third Circuit described these requirements as the "trilogy of restrictions on expert testimony: qualification, reliability and fit."

As is well known, in Daubert the Supreme Court directed district courts to perform a screening or "gatekeeping" function to insure that evidence presented by expert witnesses is relevant, reliable, and helpful to the jury's evaluation of such evidence. Daubert, 509 U.S. at 589, 597. In Kumho Tire, the Supreme Court reiterated this role and clarified that the gatekeeper function applies to all expert testimony, not only scientific testimony. Kumho Tire, 526 U.S. at 151.

A. Threshold Question of Qualification

Central to the question of admissibility, an expert witness must be qualified to testify to the opinions she intends to express. Fed. R. Evid. 702; Kumho Tire, 526 U.S. at 156. In Elcock v. Kmart Corp., 233 F.3d 734 (3d Cir. 2000), the Third Circuit reaffirmed the standard for qualifying an expert:

> Rule 702 requires the witness to have 'specialized knowledge' regarding the area of testimony. The basis of this specialized knowledge 'can be practical experience as well as academic training and credentials.' We have interpreted the specialized

> knowledge requirement liberally, and have stated that this policy of liberal admissibility of expert testimony 'extends to the substantive as well as the formal qualification of experts.'

Id. at 741 (internal citations omitted). An expert may be excluded when his training and experience is lacking in the particular area in which his testimony is offered. For example in Estate of Lam v. Upjohn Co., No. 94-0033-H, 1995 WL 478844, at *2 (W.D. Va. Apr. 21, 1995), the court excluded expert testimony on pharmaceutical warnings when the expert had "no academic training or regulatory experience and ha[d] never participated in any FDA-related proceedings addressing what constitutes an adequate warning." Thus, "a party cannot qualify an expert generally by showing that the expert has specialized knowledge or training which would qualify him or her to opine on some other issue." In re Diet Drugs Prod. Liab. Litig., No. MDL 1203, 2000 WL 962545, at *3 (E.D. Pa. June 28, 2000).

B. Unreliable Testimony Should Be Excluded

The essential guidance learned from Daubert, Kumho Tire and Joiner is that an expert's testimony must be based upon sufficient facts and flow from the reliable application of sound reasoning or methods. Fed. R. Evid. 702. "An expert's opinion is reliable if it is 'based on the "methods and procedures of science" rather than on "subjective belief or unsupported speculation"; the expert must have "good grounds" for his or her belief.'" Elcock, 233 F.3d at 745.

The non-exclusive checklist of factors set forth by Daubert and its progeny for courts to use in assessing whether a particular scientific methodology is reliable, and thereby admissible, include: (a) whether a "theory or technique…can be (and has been) tested;" (b) whether it "has been subjected to peer review and publication;" (c) whether, in respect to a particular technique, there is a high "known potential rate of error" and whether there are "standards" controlling the application of the technique; and (d) whether the theory or technique enjoys "general

acceptance" within" a "relevant scientific community." Kumho Tire, 526 U.S. at 149 (citing Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 592-94 (1993)). "The trial judge must have considerable leeway in deciding in a particular case how to go about determining whether particular expert testimony is reliable. That is to say, a trial court should consider the specific factors identified in Daubert where they are reasonable measures of the reliability of expert testimony." Id. at 152; see also Magistrini v. One Hour Martinizing Dry Cleaning, 180 F. Supp. 2d 584, 594-95 (D.N.J. 2002) (noting additional factors such as whether the expert has unjustifiably extrapolated from an accepted premise to an unfounded conclusion or whether the expert has adequately accounted for alternative explanations), aff'd, No. 02-2331, 2003 WL 21467223 (3d Cir. 2003).

Although an overused phrase, it is applicable to the testimony challenged here: "[N]othing in either Daubert or the Federal Rules of Evidence requires a district court to admit opinion evidence which is connected to existing data only by the *ipse dixit* of the expert. A court may conclude that there is simply too great an analytical gap between the data and the opinion proffered." Joiner, 522 U.S. at 146.

C. Opinions Based on Pre-Selected Data Are Unreliable

Defendants' FDA Regulatory Process experts improperly relied on a record selected by Defendants in rendering certain opinions. Thus their review was not objective and did not take into account alternate factors. In Crowley v. Chait, 322 F. Supp. 2d 530, 542 (D.N.J. 2004), one of the plaintiff's insurance industry experts based his report, in part, upon summaries of deposition testimony pre-selected by counsel. The court barred as unreliable those parts of the report which relied upon this subset of information, and admitted the report only to the extent that it was based on the expert's own independent examination of the claims files. The court, citing In re TMI Litig., 193 F.3d 613, 697 (3d Cir. 1999), stated that "[t]he information upon

which an expert bases his testimony must be reliable, and the selective furnishing of information by counsel to an expert runs afoul of Fed. R. Evid. 703, which, in addition to Rule 702, must be considered by a court for Daubert purposes." Crowley, 322 F. Supp. 2d at 542.

D. Opinions That Would Not Satisfy Daubert's Fit Requirement Should Be Precluded

In addition to reliability, Rule 702 requires that an expert's testimony assist the trier of fact in its determination of the claims and defenses. United States v. Downing, 753 F.2d 1224, 1237 (3d Cir. 1985). Lay person testimony "masquerading" as expert testimony is inadmissible. "[T]here is no more certain test for determining when experts may be used than the common sense inquiry whether the untrained layman would be qualified to determine intelligently and to the best possible degree the particular issue without enlightenment from those having a specialized understanding of the subject in dispute." Fed. R. Evid. 702 advisory committee's note (1972).

Furthermore, although an expert may opine on an ultimate issue of fact, Fed. R. Evid. 704, he "may not substitute his judgment for the jury's. "When this occurs, the expert acts outside of his limited role of providing the groundwork in the form of an opinion to enable the jury to make its own informed determination." Crowley, 322 F. Supp. 2d at 554 (precluding opinion on the credibility or consistency of other testimony and that which summarized facts) (internal citation omitted).

> Under Rules 701 and 702, opinions must be helpful to the trier of fact, and Rule 403 provides for the exclusion of evidence which wastes time. These provisions afford ample assurances against the admission of opinions which would merely tell the jury what result to reach….They also stand ready to exclude opinions phrased in terms of inadequately explored legal criteria.

Fed. R. Evid. 704 advisory committee's note; see also 29 C. Wright & V. Gold, Fed. Prac. & Pro. § 6284, at 379-80 (1997) (same).

Also, proffered opinions must flow from a sound application of methods to the facts of a casein order to be helpful. Although proponents of expert evidence do not have to "prove their case twice," they "have to demonstrate by a preponderance of evidence that their opinions are reliable." In re Paoli R.R. Yard PCB Litig., 35 F.3d 717, 744 (3d Cir. 1994). Expert opinion based on facts that are indisputably incorrect is also inadmissible, as it is both irrelevant and not helpful to the trier of fact. See, e.g., Guillory v. Bomtar Indus. Inc., 95 F.3d 1320, 1331-1332 (5th Cir. 1996) (excluding testimony based on altered forklift).

II. Challenges to Certain of Jolson's Opinions

A. Dr. Jolson's Opinion That It Was Reasonable For BMS To Believe That Vanlev Would Be Approved After OCTAVE Was Unblinded Is Inadmissible

In Section VII(E) of her expert report, Dr. Jolson discusses the meeting between FDA and BMS to discuss the unblinded results of OCTAVE. Dr. Jolson concludes that:

> BMS met with the FDA on September 21, 2002[2] to discuss the OCTAVE 24-week results. The FDA meeting minutes reflect discussion regarding the sponsor's need to make an acceptable benefit/risk argument. "The Agency pointed out that efficacy is not nor was ever an issue; 80 mg of omapatrilat lowers blood pressure better than 40 mg of enalapril. The increased incidence of [adverse events] associated with omapatrilat versus enalapril remains a concern for the Agency. The sponsor needs to show that the risk of omapatrilat is worth the benefit of the drug. The Agency needs to see the data to complete the reviews prior to making a decision or taking an action." *Based on the nature of these discussions, it was reasonable for BMS to conclude that it was potentially possible to show a favorable benefit/risk ratio based on demonstration of superior antihypertensive efficacy and the FDA's openness to consideration of this position*.

(DX 17 ¶ 133)(emphasis added).

[2] Dr. Jolson acknowledged that the September 21, 2002 citation was incorrect; the date of the meeting was September 19, 2002. (PX 29 325:17-20.)

Lead Plaintiff seeks to strike the italicized language under Daubert for the following reasons. First, her opinion is derived solely from the document itself and invades the province of the jury. When questioned about these meeting minutes, Dr. Jolson testified that:

> Q. What is your opinion or interpretation of that paragraph [of the FDA meeting minutes cited in ¶ 133 of her report], if any?
>
> * * *
>
> A. I have no opinion of it beyond exactly what it says, that they are interested in seeing the safety data and reviewing it and are interested in seeing the sponsor's risk benefit analysis.

(PX 29 285:18-25.) Her opinion would not assist the jury in any way.

Second, Dr. Jolson's opinion on this matter was based on a restricted selection of documents provided to her by defendants. She testified that she was *not* aware that the FDA had advised BMS on January 11, 2002, that if the hypertension data presented already were accurate, BMS was "already in a pretty deep hole" and it was "hard to imagine" how the heart failure data could help. (PX 29 292:8-293:17) (PX 200, which was marked as plaintiff's deposition exhibit 695) ("I haven't reviewed this document. I wasn't previously aware of it. I don't have any comment about it.")

B. Dr. Jolson's Opinion That Vanlev Was Approvable Is Inadmissible

In Section VIII of her expert report, Dr. Jolson opines that the FDA decided that Vanlev was approvable. Lead Plaintiff seeks to strike from her expert report subsection (C). In that section, Dr. Jolson opines that the FDA did not set an impossible standard for approvability in its October 11, 2002 action letter to BMS. (DX 17 ¶¶ 142-44). However, Dr. Jolson's opinion is unreliable and derived from a highly selective and inaccurate group of documents.

As background information, following the unblinding of the OCTAVE data in mid-September 2001, BMS announced that it intended to refile the Vanlev NDA for treatment of

hypertension. On December 18, 2001, BMS announced that it had refiled the Vanlev NDA for hypertension on December 14. However, Defendants did not disclose that BMS had recommended to the FDA, as part of the refiled NDA, that Vanlev receive a "black box warning" for the treatment of hypertension. Lead Plaintiff's Statement Pursuant to Local Rule 56.1 at ¶¶ 542, 567, 572-73. (hereinafter "Rule 56.1").

While the refiled Vanlev NDA was pending, BMS communicated with the FDA about the indications for which it sought approval for Vanlev. By the time the Cardiovascular and Renal Drugs Advisory Committee was convened to consider the NDA, on or about July 19, 2002, BMS was not seeking approval for broad hypertension labeling, but was only seeking approval to use Vanlev in very limited subpopulations of hypertensive patients. In addition, BMS put forward a plan for managing the risk of angioedema in this proposed limited subpopulation that was more onerous than any other plan in use for an FDA-approved drug. Five of the six members of the advisory committee voted to reject the Vanlev NDA, based on the panel's consensus assessment that the benefits of Vanlev did not outweigh its risks even in this narrowly defined subpopulation for which BMS sought approval. Rule 56.1 at ¶¶ 603-12.

The FDA accepted the advisory committee recommendations and denied approval for Vanlev on the basis of the NDA data and proposed risk management plan. Before FDA issued any official notification of its action on the NDA, BMS representatives contacted the agency to negotiate the form the rejection letter would take. On October 11, 2002, FDA issued a letter advising BMS that the Vanlev NDA was "approvable," meaning that approval might be granted after BMS conducted "at least one additional clinical trial to demonstrate an antihypertensive effect of [Vanlev] that is sufficient to off-set the identified risk of angioedema." (DX 274). In a meeting on December 6, 2002, FDA clarified that BMS could adequately demonstrate Vanlev's

utility in a resistant hypertensive population by demonstrating that Vanlev could control the blood pressure of patients who were uncontrolled in spite of treatment with four antihypertensives at maximal dose. BMS would be required to do a preliminary study to identify appropriate patients for the study proposed by FDA. BMS has not commenced such a preliminary trial. Rule 56.1 at ¶¶ 613-18.

Dr. Jolson, in her report, does not provide a full description of the October 11 FDA action letter. In that letter, the FDA advised BMS that it would need to produce "clear evidence that omapatrilat can lead to better blood pressure control in patients with resistant hypertension." In order to make that proof, it would be necessary for BMS "to conduct at least one additional clinical trial to demonstrate an antihypertensive effect of omapatrilat that is sufficient to off-set the identified risk of angioedema." (DX 274). In other words, since OCTAVE proved that Vanlev's risk of angioedema is not off-set by its benefits for the general hypertensive population, the company would now have the option of showing that the risk/benefit ratio was more favorable in patients with "resistant hypertension."

The FDA action letter suggests a possible design that would support such a showing; the FDA's proposed trial design amounts to a virtually impossible hurdle. BMS would have to:

> demonstrate a superior antihypertensive effect of omapatrilat in a patient population that has been unequivocally shown to be resistant to multiple other antihypertensives (probably at least a diuretic, angiotensin-converting enzyme inhibitor and calcium channel blocker) used in combination at their highest doses.

Id.

This trial design is virtually impossible to carry out. Elliott Levy, a senior BMS officer, testified in this case that the trial could not even be carried out until BMS had carried out a preliminary "feasibility study…more appropriately to identify appropriate sites to conduct the study." (Pl. Ex.7 129:15-130:7). There probably do not exist a substantial number of patients

who were treated with the maximum available therapy but still failed to respond. It would frankly be a wild goose chase for BMS to attempt to find a sufficient number of patients to meet the powering requirements for any credible clinical trial. (PX 16 ¶¶ 78, 79.)

Levy also said that a protocol had been written for a trial that would satisfy the FDA's requirements, but that the FDA had not approved the protocol. (Pl. Ex. 7 130:8-18.) This also reflects the practical impossibility of the project. BMS has not announced any plans to move forward with any further Vanlev trials. The "approvability letter" sets such a high bar for further trials that it is simply not possible for BMS to satisfy the agency's conditions. (PX 16 ¶ 79.)

In reaching her opinion that the FDA action letter did not set an impossible standard, Dr. Jolson testified that she did not review several BMS documents that discussed the FDA requirements. Fox example, she did not review the minutes of a meeting between BMS and the FDA held on August 28, 2002, which was designed to address issues concerning the approvability letter. (Pl. Ex. 16.) "I haven't seen this report before." (PX 29 313:22-23.) In these meeting minutes, the FDA advised BMS that:

> - FDA considers the appropriate target population to be patients that are resistant to at least three drugs from different classes used in combination at the maximum tolerated doses.
>
> - To consider an approval, FDA will need data that shows that using omapatrilat (i.e. switching the ACE inhibitor to omapatrilat) lowers blood pressure more than adding another drug (i.e., a fourth drug) to the regimen of patients in the target population.
>
> * * *
>
> - A prospective study is needed to answer the remaining questions. Dr. Temple suggested a study of patients treated and uncontrolled on three or more agents used at maximum tolerated doses randomized to a switch of the ACE inhibitor with omapatrilat or addition of a fourth drug. The patients would be randomized after a filter period in which doses of existing agents are titrated and patients are observed for

> enough time to establish that the patients were resistant. FDA said this was consistent with the Advisory Committee recommendation.

(Pl. Ex. 16, 1-2.)

Furthermore, Dr. Jolson testified that she was not aware of an internal BMS analysis following the August 28th meeting, which stated that:

> The proposed study would be extremely difficult and time-consuming to execute. A sample size of at least 1100-1400 subjects would be needed to provide adequate power to detect a difference in systolic blood pressure of 3 mmHg. To obtain these subjects, a much larger number – certainly in excess of 10,000 – would need to be enrolled.
>
> The proposed study would not provide meaningful information about the efficacy of omapatrilat in the proposed target population. Because the number of antihypertensive agents would not be the same in the two treatment groups, the effect of omapatrilat could not be discerned.
>
> The proposed study would not provide meaningful information about the therapeutic alternatives available to physicians and patients. The comparison group would receive guanfacine, which is rarely used. Even if a more commonly used antihypertensive were substituted for guanfacine, the study would provide information about only one therapeutic alternative. No study, or group of studies, could provide information about each of the dozens of alternative antihypertensives available.

(Pl. Ex. 26 at VAS0 0232660.) Dr. Jolson testified that "I haven't seen this document." (PX 29 317:8.)

Dr. Jolson also testified that she had not seen an internal BMS memo between Elliott Levy and Elliot Sigal that the "FDA has taken an extremely hard regulatory stance."

> Throckmorton requested that we conduct a study in which patients with substantially elevated blood pressure on three or more drugs from different classes at maximal tolerated doses be randomized either to substitute omapatrilat for the RAS active drug in their regimen, or add a fourth drug. Guanfacine 1 mg was suggested by Bob Temple as the add-on drug in the comparison group.

> This study has two objectives: to prove that omapatrilat works in the target population, and to prove that nothing else does. The latter objective reflects a significant hardening in the FDA position. At the Advisory Committee, Throckmorton suggested that patients uncontrolled on three drugs could be regarded as resistant. He is now requesting empiric proof, in the form of a trial on a fourth agent.
>
> Lacking a single, clear objective, this study is of questionable scientific validity and will be difficult to interpret. *Perhaps more important, it cannot succeed*.

(Pl. Ex. 27.) (emphasis added.) Dr. Jolson testified, "I just don't have a recollection of having seen it." (PX 29 320:21-22.)

Most importantly, Dr. Jolson has no concept of how many people even meet this target population; that is, how many people with hypertension do not have their blood pressure controlled after taking *four* medications at the highest dosage.

> Q. Are you aware of what percentage of people in the United States with hypertension have been shown resistant to four antihypertensives at maximumly tolerated doses?
>
> A. No, I'm not aware of that information.
>
> Q. Do you have any understanding as to how easy or difficult it would be to enroll patients who met that criteria?
>
> A. Again, I don't have information about how many of these patients would be available according to his definition.
>
> Q. Or what the universe of such patients would be in the United States?
>
> A. I don't have direct knowledge that would tell me how many of these patients are available.

(PX 29 319:5-24.)

As BMS acknowledged internally, the FDA action letter sets forth an impossible standard exactly because the Company could not identify a sufficient number of patients in this target

population to even construct a clinical trial. Yet Dr. Jolson has no knowledge of this crucial information.

Accordingly, Dr. Jolson should not be allowed to testify on this issue.

III. Challenges to Certain Anderson Opinions

A. Dr. Anderson Should Be Precluded From Opining As To What Inferences, If Any, Can Be Drawn From The Fact "That The FDA Continued To Offer BMS Priority Review Status" Based on His Qualifications

Dr. Anderson asserts in his report that because the FDA did not rescind BMS's priority review status for the initial NDA, that is evidence that the FDA did not believe it was misled by BMS. (DX 11 ¶ 27.) But this testimony is beyond the scope of his expertise, as his own testimony confirms. Dr. Anderson is a Professor of Internal Medicine (Cardiology) at the University of Utah School of Medicine and an Associate Chief of Cardiology at LDS Hospital. (DX 11 ¶ 1.) He has been a member of the Cardio Renal Advisory Committee, which advises the FDA on proposed drugs, and has been a clinical trial investigator. (DX 11 ¶ 3-4, Pl. Ex. 1 17:11-18:10).

However, he has never worked for the FDA. (DX 11, Ex. A.) He has done no research or analysis to determine what regulatory mechanism, if any, exists for changing a priority review application to a standard review application, nor is he aware of what the criteria are, if any, for changing a priority review application to a standard review application. (Pl. Ex. 1 103:9-23.) Moreover, he had no regulatory responsibility for any priority review applications while employed with Merck, and he has no recollection of any priority review applications coming before him while he was on the CardioRenal Advisory Committee. (Pl. Ex. 1 104:25-106:7.)

His opinion about priority review is simply based on anecdotal evidence and observations that FDA has discretion, regardless of its regulations, to revoke priority review. (Pl. Ex. 1 104:8-

24.) Accordingly, any testimony offered by Dr. Anderson about priority review issues should be precluded.

B. Dr. Anderson is Not Qualified to Opine on Genetics

Dr. Anderson's curriculum vitae makes it abundantly clear that he is a cardiologist by training and practice. (DX 11, Ex. A.) He confirmed as much at his deposition. (Pl. Ex. 1 8-9, 16-19, 24-25.) Yet, venturing to a discipline beyond his expertise, Dr. Anderson stated in his report that "genetics *appears* to contribute to the tendency of a particular patient to develop angioedema. Identification of genetic factors that underlie predisposition to angioedema *might* permit pre-screening of patients to totally avoid this risk in the future while allowing the great majority to benefit by this therapeutic advance." (DX 11 ¶37) (emphasis added). Dr. Anderson has not held himself out to be an expert in pharmacogenetics or pharmacogenomics, and thus should not be permitted to offer expert opinions about genetics. Moreover, this testimony is highly speculative as stated and as explained at Dr. Anderson's deposition. (Pl. Ex.1 266:3-24.) He has no basis for it aside from one article that he could not name, did not cite in his report or provide to Lead Plaintiff. Id.

C. Certain of Dr. Anderson's Opinions Are Unreliable Because They Are Not Based on Sufficient Facts

1. Dr. Anderson Cannot Opine That The FDA Had "An Overall Favorable Interpretation Of Benefit/Risk" With Omapatrilat

In his report, Dr. Anderson states that the FDA had "an overall favorable interpretation of benefit/risk" with respect to Vanlev. (DX 11 ¶ 28.) First, there is simply no basis for Dr. Anderson to purport to know what the FDA thought about Vanlev. A witness cannot testify to another's state of mind. Roberson v. City of Philadelphia, No. 99-3574, 2001 WL 210294, at *7 (E.D. Pa. Mar. 1, 2001) (expert could not opine on whether a third-party or their friends feared arrest). Second, and contrary to Fed. R. Civ. P. 26(a)(2)(B), there is no support for this

proposition in his report or in the documents that he reviewed. The statement itself is void of documentary support, and at his deposition Dr. Anderson could point to no supporting documents. (Pl. Ex. 1 98:7-99:7.) Moreover, Dr. Anderson admitted he spoke with no member of the FDA Advisory Committee that considered the Vanlev application, nor with any current or former FDA employee about Vanlev. (Pl. Ex. 1 87:4-24.) Indeed, when pressed, Anderson himself suggested a "modification" to his report to the effect that there was "the possibility of overall favorable benefit/risk, pending a formal review." (Pl. Ex. 1 98:7-23.)

Thus, all we are left with is the "possibility" that a new drug application might have a favorable risk/benefit profile. That is not well grounded expert opinion and it will not be helpful for the trier of fact to hear Dr. Anderson's rank speculation.

2. Dr. Anderson Should Not Be Allowed to Opine on the FDA's State of Mind with Respect to Squibb's NDA for Captopril, Particularly Since The Testimony Is Based Solely on Hearsay

In his report, Dr. Anderson discusses the drug approval process with respect to the Squibb (BMS's predecessor) product Captopril, the first ACE-inhibitor approved by the FDA. (DX 11 ¶ 30.) In doing so he conveys the FDA's internal thinking with respect to the application, e.g., "[t]he FDA, *though concerned*, also *was impressed* with the potential for captopril to offer unique benefits in hypertension and heart failure. Based on these considerations and encouragement from FDA, Squibb did further trials and supplemented its NDA." Id. (emphasis added).

As support, it was revealed at his deposition that Dr. Anderson relies solely on a conversation with a "Dr. Erreich" (conveniently arranged by defense counsel) to inform him as to the "specific reaction" and "internal workings" of the FDA with respect to the Captopril NDA. (Pl. Ex. 1 77:8-80:20; 83:2-84:4.) This is impermissible hearsay. "To be sure, an expert may not be used simply as a vehicle for the admission into evidence of otherwise inadmissible hearsay

testimony." Crowley v. Chait, 322 F. Supp. 2d 530 (D.N.J. 2004); see also 29 C. Wright & V. Gold, Fed. Prac. & Pro. § 6273, p. 312 (1997) ("Rule 703 does not authorize admitting hearsay on the pretense that it is the basis for expert opinion when, in fact, the expert adds nothing to the out-of-court statements other than transmitting them to the jury.")

Moreover, there is no factual support for this opinion—even leaving aside the general problem of a witness testifying to someone else's state of mind. Dr. Anderson did not know what role Dr. Erreich played in the development or approval process for Captopril. He did not know whether Dr. Erreich had any review responsibilities for Captopril "other than that as an inside person he was familiar with the general . . . sort of the general occurrence of events." (Pl. Ex. 1 84:5-85:21.) Dr. Anderson could not even identify what title Dr. Erreich held with the FDA while the Captopril NDA was ongoing. Id. Moreover, Dr. Anderson confirmed at his deposition that he reviewed no correspondence between the FDA and Squibb with respect to the Captopril NDA. (Pl. Ex. 1 88:7-89:10.)

To the extent Dr. Anderson has any support for his statements with respect to the mindset of the FDA about captopril, it has certainly not been shown to be reliable. Thus Dr. Anderson should be precluded from testifying as to the FDA's state of mind in connection with Squibb's experience with Captopril.

D. Certain of Dr. Anderson's Opinions Are Unreliable Because They Are Based on Pre-Selected Data

Dr. Anderson improperly relied on a record selected by Defendants to form certain opinions. Thus his review was not objective and did not take into account alternate factors. In Crowley v. Chait, 322 F. Supp. 2d 530, 542 (D.N.J. 2004), one of the plaintiff's insurance industry experts based his report, in part, upon summaries of deposition testimony pre-selected by counsel. The court barred as unreliable those parts of the report which relied upon this subset

of information, and admitted the report only to the extent that it was based on the expert's own independent examination of the claims files. The court, citing In re TMI Litig., 193 F.3d 613, 697-98 (3d Cir. 1999), stated that "[t]he information upon which an expert bases his testimony must be reliable, and the selective furnishing of information by counsel to an expert runs afoul of Fed. R. Evid. 703, which, in addition to Rule 702, must be considered by a court for Daubert purposes." Crowley, 322 F. Supp. 2d at 542.

1. Dr. Anderson Should Not Be Permitted To Testify That "Statements Such as 'The Side Effect Profile of Omapatrilat Is Similar to the ACE Inhibitors' Were Reasonable Prior to OCTAVE"

In his report, Dr. Anderson states that "the early clinical trial data, though suggesting the potential for angioedema with omapatrilat, did not indicate a differential risk of angioedema with omapatrilat above that of other ACE inhibitors. Hence, statements such as 'the side effect profile of omapatrilat is similar to the ACE inhibitors' were reasonable prior to OCTAVE." (DX 11 ¶ 22.) At his deposition, however, he was given the opportunity to review PX 53 (OMA 0078119-141), the April 4, 2000 Secondary Review written by FDA Reviewer Dr. Norman Stockbridge, a document not provided to him by defense counsel. (See DX 11, Ex. B.) PX 53 details the cases listed as angioedema in the pre-OCTAVE omapatrilat clinical trials. Upon reviewing PX 53 (identified in the transcript as Plaintiffs' deposition exhibit 34), Dr. Anderson acknowledged that the data from the trials "does raise [the] question" as to whether the pre-OCTAVE trials showed a differential risk of angioedema with omapatrilat relative to other ACE-inhibitors, and that it was evidence of the possibility that omapatrilat was associated with a greater incidence of angioedema than ACE-inhibitors. (Pl. Ex. 1 278:3-279:9.) Inasmuch as Dr. Anderson disavowed the factual predicate for his belief that "statements such as 'the side effect profile of omapatrilat is similar to the ACE inhibitors' were reasonable prior to OCTAVE," his opinion as inadmissible.

2. Dr. Anderson's Opinions With Respect To The FDA's Views Of The Post-OCTAVE NDA Are Uninformed

In his report, Dr. Anderson states: "After OCTAVE, the FDA reaffirmed Vanlev's potential for approval when it invited BMS to file a new NDA. This encouragement is notable, and it rightly supported BMS's optimism about Vanlev." (DX 11 ¶ 38, n.13 (citing OMA1727589-592 as support for first quoted sentence.) The document in question, the sole basis for Anderson's opinion, sets forth minutes from a September 2001 meeting between BMS and the FDA. (DX 64.) The minutes do not memorialize any "invitation."

Putting aside for the moment the reasonableness of Dr. Anderson's assertion that this document evidences any reaffirmation or encouragement on the FDA's part, his opinion must also be precluded because he was not afforded the opportunity to look at all relevant documents with respect to this meeting. It appears that Defendants' counsel chose to omit from the materials sent to Dr. Anderson another document that puts a vastly different cast on what FDA personnel thought of the OCTAVE data discussed at the September 2001 meeting. Plaintiff's summary judgment exhibit 200 (plaintiff's deposition exhibit 695) is a BMS record of contact with the FDA in January 2002. (PX 200.) It memorializes that in a telephone conversation with a BMS employee, Dr. Norman Stockbridge, the FDA's medical team leader with respect to the Vanlev application, informed BMS that "if the hypertension data presented already [i.e., in September 2001] were accurate, 'we were in a pretty deep hole,' and it was 'hard to imagine' how the heart failure data could help." Dr. Anderson's opinion is thus woefully uninformed -- apparently by design -- and would be of no help to the finder of fact.

IV. Challenges to Certain Fredd Opinion

A. Certain of Dr. Fredd's Opinions Are Unreliable Because They Are Not Based on Sufficient Facts

Dr. Fredd explains in his report that the purpose of his testimony is "to address the regulatory process for the review of a New Drug Application ("NDA") by FDA, and on [the FDA Division of Cardio-Renal Drug Products'] review of the NDA for Vanlev." (DX 13 ¶ 11.) With respect to the first topic – the typical regulatory process of an NDA review – Lead Plaintiff does not contest Dr. Fredd's ability to speak generally on mechanics of an NDA process flow.

However, with respect to the latter purpose of Dr. Fredd's testimony – the Division of Cardio-Renal Drug Products' review of Vanlev – Dr. Fredd can be described either as a fact witness without personal knowledge of the relevant facts or an expert witness without relevant expertise. Either way, the entirety of his testimony concerning the FDA process as it relates specifically to Vanlev is inadmissible and should be precluded.

1. Dr. Fredd Cannot Opine on the Initial Vanlev NDA Review Process

Dr. Fredd acknowledged that he had "no official involvement in the review" of Vanlev. (PX 26 25:4-8.) His only "unofficial" involvement with the initial Vanlev NDA was having a few conversations with FDA's Dr. Norman Stockbridge, who was reviewing the Vanlev NDA, in early 2000 concerning the four Vanlev subjects who required, in Dr. Fredd's words, "mechanical airway patency, to maintain a patent airway". (PX 26 26:4-24.) The essence of those conversations was that there were four such subjects and Dr. Stockbridge said he had "not seen this number of cases before in a dossier for approval of an ACE inhibitor." (PX 26 26:15-17.) See also PX 26 30:8-14. (Dr. Fredd had no Vanlev-related discussions "with Drs. Temple, Fenichel, Lipicky, Pelayo, the statistician or anyone else" at FDA).

Moreover, Dr. Fredd also admitted during his deposition that he had "ambiguity" as to process flow of the Vanlev NDA because it was given priority review. (PX 26 41:12-42:5.) Accordingly, there is no basis for Dr. Fredd to opine about anything specifically related to the review process of the initial Vanlev NDA. Dr. Fredd's testimony must be limited to his knowledge of the NDA process generally.

2. Dr. Fredd Cannot Opine on What FDA's Dr. Temple Would Or Would Not Have Thought or Said About Vanlev

Dr. Fredd's lack of knowledge of or involvement in the Vanlev NDA review process extends to the post-OCTAVE era as well. Dr. Fredd did not attend the Vanlev advisory committee meeting in July 2002. (PX 26 132:21-25.) After the July 2002 advisory committee meeting, Dr. Fredd never discussed with Dr. Temple, the Director of the FDA's Office of Drug Evaluation I, the issue of what might satisfy Dr. Temple such that the Vanlev NDA could be approved. (PX 26 123:10-19.) Nor was Dr. Fredd at any meetings between BMS and Dr. Temple discussing the "approvable" letter. (PX 26 114:4-7.)

Yet that dearth of communication or involvement did not stop Dr. Fredd from opining on what Dr. Temple thought. In his expert report, Dr. Fredd states that "[a]t the Vanlev advisory committee meeting, Dr. Tom Fleming's analysis and discussion of the data . . . would carry great weight with Dr. Temple as he came to render his final decision on the NDA." (DX 13 ¶ 34.) There is simply no basis, either factually or legally, upon which to allow Dr. Fredd to testify that one 15-line passage from a 294-page transcript "would carry great weight" with Dr. Temple. (See, PX 389 at 259-60.) Indeed, at his deposition Dr. Fredd unintentionally acknowledged the absurd degree to which his "expertise" as a former FDA official was being stretched:

> So my reading of what Dr. Temple was saying during the advisory committee and my reading of his letter makes me conclude that he concluded, although I'm reading his mind, you know, and I'm

> interpreting what he is saying based on my long experience of working with him, that those were his conclusions.

(PX 26 113:18-24) (emphasis added). Later in the deposition Dr. Fredd tried to bolster his unique ability to convey the inner workings of Dr. Temple's mind by volunteering that he was "very sensitive to Dr. Temple's writing." (PX 26 123:24-25.)

Dr. Fredd's report and testimony go beyond a garden variety attempt to admit hearsay and "state of mind" evidence through an expert. This is more along the lines of Defendants using Fredd as a surrogate for one of the Vanlev NDA reviewers. It is wholly improper and he should not be allowed to testify about what the FDA, or anyone at the FDA, knew, thought or said about Vanlev or the review of the Vanlev NDA.

3. Dr. Fredd Is Not Competent to Testify on the Feasibility of the Clinical Trial Discussed in the FDA's Approval Letter

In his report, Dr. Fredd asserts that "[c]ontrary to lead plaintiffs expert Dr. Robert Nelson (see pp. 78-79), a study in resistant hypertension is a feasible study, and the approvable letter included an offer by FDA to assist the company in designing the study." (DX 13 ¶ 97.) Dr. Fredd does not have the expertise necessary to make that determination. At his deposition, when discussing the FDA's October 11, 2002 "action" letter, he admitted that he had "[n]ot a very good" understanding of what the term "patients with resistant hypertension" meant and that he was "not an expert in hypertension". (PX 26 136:2-10.) Dr. Fredd then testified as follows:

> Q. Do you have an understanding of how difficult it would be to conduct a test that Dr. Temple talked about in the approvable letter?
>
> A. He does not talk about a specific test. He writes invites discussions with the company.
>
> * * *

> Q. With the design that is identified in the letter, do you have any basis for saying one way or the other how difficult or easy it would to be conduct such a test?
>
> A. I have no basis for knowledge of that.

(PX 26 136:24-137:4, 137:25-138:5.) As Dr. Fredd admitted he had a poor understanding of the relevant patient population and no basis for knowing how difficult or easy it would be to conduct the test discussed in the FDA's "action" letter, he has no basis on which to opine that such as study is feasible. This testimony must be stricken.

4. Dr. Fredd's Opinions on the "Pendulum Swing" at FDA Affecting the Review of the Vanlev NDA Are Without Basis

One of the core conclusions of Dr. Fredd's report centers on "pendulum" swings in FDA attitudes that occurred in the 1990s, and how those changes in attitudes impacted the Vanlev NDA process: "At times FDA is more risk averse than at other times. I conclude that at the time [the Division of Cardio-Renal Drug Products] was reviewing the Vanlev NDA, it was more risk averse than it had previously been." (DX 13 ¶ 14.) More specifically, Dr. Fredd claims that a single event – the June 1998 withdrawal of the drug Posicor from the market – had a "sudden and profound" impact on the Division of Cardio-Renal Drug Products. (DX 13 ¶ 62.) Dr. Fredd has no basis for claiming that the FDA's experience with Posicor had any effect whatsoever on its review of the Vanlev NDA. His testimony therefore must be stricken.

(a) Dr. Fredd's Opinion Is Based on Incorrect Facts

As an initial matter, Dr. Fredd has his facts wrong. "Expert opinion based on facts that are indisputably incorrect is inadmissible, as it is both irrelevant and not helpful to the trier of fact." See, e.g., Guillory v. Harlo Prod. Corp., 95 F.3d 1320, 1331-1332 (5th Cir. 1996) (excluding testimony based on altered forklift).

Dr. Fredd points to the "Tasosartan example" as an event that "exemplif[ied] the attitudinal shift to a risk averse position" that followed the June 1998 withdrawal of Posicor from the market. (DX 13 ¶ 66-68.) Tasosartan, he explains, was an antihypertensive drug never approved by FDA because of concerns about liver damage—even though the FDA advisory committee considering the drug voted in favor of its approval given its efficacy. He also states that the "Tasosartan NDA decision process was contemporaneous with the review of the Vanlev NDA" (DX 13 ¶ 67), implicitly suggesting that in the post-Posicor withdrawal environment, otherwise meritorious NDAs, like those for tasosartan and Vanlev, languished. When asked at his deposition "Can you tell me why it is that your views concerning the Posicor influence on the individuals who reviewed the NDA for VANLEV isn't simply speculation on your part" the following exchange occurred:

> A. I think it is my expert judgment. You may characterize it as speculation.
>
> Q. Can you tell me why it is that it is expert judgment as opposed to speculation.
>
> A. Because I think it's based on some facts.
>
> Q. And what particular facts?
>
> A. I tried to lay them out in my expert review. Look at what happened to Labetalol, a beta blocker for hypertension which offered nothing in terms of an increased benefit and had as much hepatitis risk or liver enzyme abnormality risk as tasosartan did [but it was approved pre-Posicor].
>
> And Dr. Temple remarked in one of the meetings that in old -- in other days we have approved a drug with an increased risk with very mild labeling, but they never did that same thing with tasosartan, *so it seemed to me in the tasosartan experience, in spite of a recommendation by the advisory committee to approve tasosartan, that that is consistent with my view*.
>
> * * *

Q. Labetalol was a drug that was approved when?

A. I believe 1985.

(PX 26 80:10-81:15) (emphasis added).

The only problem with this "consistent" view is that it is inconsistent with the facts. On March 3, 1998, fully three months before the Posicor withdrawal, Wyeth-Ayerst "announced it is withdrawing its new drug application (NDA) for Verdia® (tasosartan) Capsules. This action is the result of an unresolved question arising from ongoing discussions with the Food and Drug Administration (FDA) regarding the safety profile." See http://www.wyeth.com/news/Pressed_and_Released/pr03_03_1998.asp?archive=1998 (last visited 5/10/05).

Dr. Fredd used the "tasosartan example" as key factual support for his opinion that the Posicor withdrawal caused a "sudden and profound" impact on the risk-benefit decisions in the Division of Cardio-Renal Drug Products during the Vanlev NDA. Because the tasosartan NDA was withdrawn from the FDA's consideration before Posicor was withdrawn from the market, Dr. Fredd's reliance on tasosartan to support his opinion as to the importance of Posicor is entirely misplaced. As such, any testimony offered by Fredd concerning Posicor's impact, based as it is on incorrect facts, is unreliable and inadmissible.[3]

(b) Dr. Fredd Has No Factual Support For His Opinions

The "sudden and profound" impact that Posicor had on the FDA's Division of Cardio-Renal Drug Products was not memorialized in any FDA document to which Dr. Fredd could point. Dr. Fredd took no relevant documents with him when he left FDA, there were no FDA

[3] Indeed if, as Dr. Fredd claims, the "tasosartan example" evidences a shift in FDA attitudes towards a more risk averse position, then it is hardly an example that helps Defendants. Wyeth-Ayerst's very public withdrawal of that antihypertensive's NDA because of an "unresolved question . . . regarding the safety profile" occurred more than a year-and-a-half before BMS filed its NDA for Vanlev.

documents that helped inform the opinions in his report, and he does not have access currently to non-public FDA documents. (PX 26 20:21-22:3.)

Nor was this alleged impact the subject of contemporaneous conversations he had concerning how the Posicor withdrawal affected the Vanlev review process. Dr. Fredd never had any conversations about the Vanlev review process other than the few conversations with Dr. Stockbridge discussed above concerning the four Vanlev subjects who had been intubated. He recalls no other conversations with anyone else at the FDA concerning Vanlev. (PX 26 27:17-21, 30:8-14.) Indeed, Dr. Fredd further admitted that he never discussed with either Dr. Fenichel, the deputy director for review at the time of the initial Vanlev NDA, or Dr. Stockbridge, the medical "group leader" for the initial Vanlev NDA, the impact that the Posicor withdrawal had on either of them. (PX 26 65:20-66:6, 37:3-6, 25:14-15.) Nor did he ever have any conversations with either of them, or with Dr. Lipicky, the Director of the Division of Cardio-Renal Drug Products, with respect to lessons learned from the Posicor experience. (PX 26 83:19-23.)

It is thus inconceivable that Dr. Fredd can speak with any authority whatsoever on the issue of what effect, if any, the Posicor withdrawal had on the Vanlev NDA review process. (Cf. PX 26 55:6-56:9 (Dr. Fredd admitting that he "cannot speak for other medical reviewers" concerning whether or not published medical literature concerning a drug under NDA review influences the decision-making of FDA reviewers).)

(c) Dr. Fredd Cannot Be A Vehicle for Inadmissible Hearsay

Further on the subject of Posicor, Dr. Fredd discusses in his report "a series of articles" written by David Willman and published in the Los Angeles Times, and a particular email response to Mr. Willman's articles by Dr. Fenichel. (DX 13 ¶¶ 51-54.) If either the articles or email Dr. Fredd mentions have a legitimate basis for being admitted into evidence in this

litigation then Defendants can seek to offer them in evidence. (Dr. Fenichel's e-mail is available on his personal website. See http://www.fenichel.net/pages/Professional/subpages/la_times.htm (last visited 5/10/05). In this instance, Dr. Fredd is nothing more than a vehicle through which this inadmissible hearsay is sought to be introduced. Thus, Dr. Fredd should be precluded from testifying as to the articles and Dr. Fenichel's email.

5. Opinions Stemming From Dr. Fredd's Inadmissible Posicor-Related Opinions Must Be Precluded

As discussed above, Dr. Fredd's opinions concerning attitudinal shifts at the FDA, and their alleged impact on the FDA's review of Vanlev, must be precluded. By extension, the further conclusions Dr. Fredd draws based on those inadmissible premises must also be precluded.

In particular, Dr. Fredd links "attitudinal shifts at division level" to "a reconsideration of blood pressure . . . reduction as a surrogate for a clinical benefit for antihypertensive drugs." (DX 13 ¶ 58.) Because Dr. Fredd's opinions concerning shifts in attitude at FDA are themselves inadmissible, he must be precluded from testifying that attitudinal shifts had a causal relationship to any FDA statements on the use of blood pressure reduction as a surrogate measure of the clinical benefit of an antihypertensive medication. See, e.g., PX 26 ¶¶ 62-63 (discussing Posicor withdrawal and suggesting it prompted discussion at a March 17, 2000 meeting between BMS and FDA concerning the acceptability of using the surrogate endpoint of blood pressure reduction to approve antihypertensive agents). Dr. Fredd's testimony on what the FDA may have thought or believed concerning the acceptability of surrogate endpoints in connection with the Vanlev NDA is based on nothing other than his own speculation. Therefore all such testimony must be precluded.

V. Defendants Should Be Required to Choose One of Their Three "FDA Regulatory Process" Experts Because Their Proffered Testimony is Cumulative and Repetitive

Defendants' three designated "FDA Regulatory Process" expert witnesses offer overlapping and cumulative opinions in the area of regulatory process, the FDA's review of the Vanlev NDAs, BMS's regulatory compliance, the OCTAVE trial and whether Vanlev was approvable. Because such repetitive testimony is a classic example of needlessly cumulative, time-wasting and unfairly prejudicial evidence, Defendants should be required to choose one expert to testify about these matters.

In In re Paoli R.R. Yard PCB Litig., 35 F.3d 717, 746 (3d Cir. 1994), the Third Circuit reaffirmed that "under Rule 702, admissibility of scientific testimony turns not only on reliability but also on the possibility that admitting the evidence would overwhelm, confuse, or mislead the jury"; and that Rule 702 partly incorporates Rule 403 analysis with respect to experts. See also Planned Parenthood v. Verniero, 22 F. Supp. 2d 331, 338-43 (D.N.J. 1998)(Hughes, N.J.) (excluding 10 of defendants' 14 expert witnesses as irrelevant, unnecessary and cumulative pursuant to Fed. R. Evid. 402, 403, 611 and Fed. R. Civ. P. 1 and 16).

> Multiple expert witnesses expressing the same opinions on a subject *is a waste of time and needlessly cumulative.* It also raises the possibility that jurors will resolve competing expert testimony by *"counting heads"* rather than evaluating the quality and credibility of the testimony.

Sunstar, Inc. v. Alberto-Culver Co., No. 01 C 0736, 2004 WL 1899927, at *25 (N.D. Ill. Aug. 23, 2004) (emphases added). Here:

- All three experts give an overview of the U.S. regulatory process. Compare (DX 17 ¶ 29-81 (Jolson); DX 13 ¶ 19-46 (Fredd); DX 11 ¶ 29-31 (Anderson).)
- All three experts discuss and opine on BMS's compliance with FDA regulations. Compare (DX 17 ¶ 85-114 (Jolson); DX 13 ¶ 81-90 (Fredd); DX 11 ¶ 25-28, 39-40 (Anderson).)

- All three experts discuss and opine on the FDA's review of the Vanlev NDA. Compare (DX 17 ¶ 115-119 (Jolson); DX 13 ¶ 60, 63-66, 69-71, 96 (Fredd); DX 11 ¶24-28 (Anderson).)

- All three experts discuss and opine on the OCTAVE trial. Compare (DX 17 ¶ 120-132 (Jolson); DX 13 ¶ 38, 89-90 (Fredd); DX 11 ¶ 32-37, 43-44 (Anderson).)

- All three experts opine on whether the Vanlev NDAs were approvable. Compare (DX 17 ¶ 115-119, 133-144 (Jolson); DX 13 ¶ 59, 69-80, 91-98 (Fredd); DX 11 ¶ 15-23, 36-38, 41-42 (Anderson).)

- All three experts discuss whether Vanlev would have required a "black box" warning. Compare (DX 17 ¶ 145-147 (Jolson); DX 13 ¶ 98 (Fredd); DX 11 ¶ 45-46 (Anderson).)

- Drs. Jolson and Fredd discuss how the FDA can be, and was during Vanlev's review, more "risk averse." Compare (DX 17 ¶ 82-84 (Jolson); DX 13 ¶ 47-58, 61-68 (Fredd).)

Lastly, Drs. Jolson and Fredd also both discuss the meaning of the phrase "airway compromise" and give assessments of how BMS used the phrase. (DX 17 ¶ 100 (Jolson); (DX 13 ¶ 16, 73 (Fredd).) Their discussions of airway compromise are duplicative of the opinions expressed by Defendants' two "airway compromise" experts, Dr. Murphy and Walls, and should be precluded as discussed in the motion directed at Drs. Murphy and Walls' expert opinion, also submitted herewith.

CONCLUSION

For the reasons set forth above, Lead Plaintiff respectfully requests that the Court grant the instant motion to strike portions of Drs. Jolson's, Fredd's and Anderson's expert reports.

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